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# French national addictovigilance follow-up of zolpidem between 2014 and 2020: evolution of drug abuse, misuse and dependence before and after the regulatory change

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**Background:** Since the appearance of zolpidem on the market, the occurrence of serious cases of abuse, misuse and dependence have come to the attention of authorities. In view of the increase in the number and severity of cases among zolpidem users and the predominant presence of zolpidem in falsified prescriptions, the French Health Authorities implemented part of the narcotics regulation for zolpidem in April 2017. The objective of this article was to describe the evolution of the abuse, dependence and misuse of zolpidem. **Methods:** We used three data sources: (i) zolpidem is a reimbursable and strictly prescription drug in France. Medic’AM is a public database that indicates the number of tablets reimbursed each month in France for each reimbursable drug. This database has been analyzed as a proxy of the exposure of the French population to zolpidem; (ii) all French cases of drug dependence or abuse reported by health professionals (regulatory obligation) and (iii) an epidemiological tool based on the surveillance of falsified prescriptions over two periods: the 3-year period before the regulatory measure (2014–16) and the 3-year period after the regulatory measure (2018–20). **Results:** This regulatory change had two immediate consequences: a sharp decline in falsified prescriptions and a decrease of ~57% between the two study periods in the zolpidem reimbursement data. Markers of problematic consumption remained after the regulatory change with worsening cases, particularly for people who were genuinely dependent and/or had comorbidities or misusers for whom zolpidem was the substance of interest, whose proportion increased significantly in the addictovigilance notification system, from 43.6% ( $N = 107$ ) to 59.3% ( $N = 127$ ) ( $P < 0.01$ ). **Conclusions:** Further monitoring is needed in light of these persistent markers of problematic consumption.

## Introduction

In France, there is a special system coordinated by the ANSM (French Drug Agency) called Addictovigilance, which collects and analyzes cases of abuse or dependence related to the use of psychoactive substances.<sup>1,2</sup> It uses (i) notifications of cases of drug dependence or abuse from health professionals (NOTS, for spontaneous notifications in French); in France, health professionals have a regulatory obligation to report cases to their centre<sup>3</sup> and (ii) epidemiological surveillance tools, including OSIAP (Suspect Prescriptions Possibly Indicating Abuse), which is based on the surveillance of falsified prescriptions presented in community pharmacies.<sup>2,4</sup>

Zolpidem is a non-benzodiazepine hypnotic that is indicated for the treatment of transitory or occasional insomnia. It is a positive allosteric modulator of rapid inhibitory neurotransmission of GABA at GABA-A receptors and has the particularity of binding specifically to the alpha-1 subunit of these receptors.<sup>5</sup> Since it appeared on the market, the occurrence of serious cases of abuse and dependence

have alerted the authorities, and an addictovigilance follow-up has been set up, coordinated by the Nantes centre. This follow-up studying the data since 1993 highlighted two distinct populations among users: one of chronic users who take the drug for sedation but given the short half-life of zolpidem use several doses during the night for hypnotic purposes; a second population that seeks an effect other than hypnotic, mostly stimulant, that takes zolpidem during the day and uses massive doses and obtains zolpidem in fraudulent ways, including falsifying prescriptions.<sup>6</sup> These data were confirmed during follow-up and in the context of pharmacoepidemiology work.<sup>7–11</sup> The severity of cases led to a modification of the Summary of Product Characteristics (SPC) of zolpidem warning against the risk of dependence starting in 2003.<sup>6,12</sup>

Despite this modification, the situation has worsened: with average doses consumed above 100 mg per day, and the consumption of doses >1 g per day. The population that seeks positive effects identified in the first study was found in all further national studies,<sup>7</sup> and the proportion of users who consume zolpidem by a route other than the oral route increased from 6% in 2003–10 to 9–15% between 2010

and 2020. In view of the increase in the number and severity of cases of abuse and dependence among zolpidem users, as well as the persistence of the two distinct populations,<sup>7</sup> the unprecedented presence of zolpidem in falsified prescriptions reported to the French Addictovigilance Network (FAN) (first molecule cited, zolpidem was on about a third of the falsified prescriptions reported to the FAN before 2017), the French health authorities informed physicians in January 2017 of the implementation of part of the narcotics regulations for zolpidem-based drugs.<sup>13</sup> Zolpidem must now be prescribed with a secure, tamper-proof method. The measure was implemented in April 2017.

The objective of this article was to present the evolution of the abuse, dependence and misuse of zolpidem in French addictovigilance data since the implementation of the regulatory measure.

## Methods

### Study oversight

This study was a national study using three data sources:

- Medic'AM open data provided by the French national health care system. Medic'AM is a public database that indicates the number of tablets reimbursed each month in France for each reimbursable drug. Zolpidem is a reimbursable and strictly prescription drug in France. Medic'AM has been analyzed as a proxy of the exposure of the French population to zolpidem.
- NOTS: French records of dependence or abuse cases reported by health professionals and collected by the FAN. An addictovigilance notification includes sociodemographic data, medical history and coconsumption and data on the products consumed and on the consumption, including: quantity, duration, route of administration, search effects and method of obtention. In this analysis, we focused only on the NOTS that mentioned zolpidem as a 'suspected' substance. The notifications are analyzed by medical pharmacologists working in the addictovigilance centres. Reports are then recorded in the French national database.

Data from the epidemiological survey OSIAP, which is a national programme that continuously collects and analyzes falsified or forged prescriptions presented by patients in French community pharmacies. OSIAP relies on spontaneous reports: in France, pharmacists are not mandatory to declare falsified prescriptions presented to them to the FAN.<sup>4</sup> OSIAP ranks the most frequently identified drugs on falsified prescriptions. For this study, we analyzed the positioning of zolpidem among the other most frequently cited drugs.

### Study procedure

Two study periods were defined: the 3-year period before the measure was implemented, ranging from January 2014 to December 2016, and the 3-year period after the measure, ranging from January 2018 to December 2020. Data from January to December 2017, the transition year in which the regulatory announcement (January) and change (April) occurred, were not included.

## Outcomes

### Zolpidem NOTS volume and importance

- The number of annual notifications received in the addictovigilance system between 2014 and 2020, including zolpidem as a suspected drug, was used. We related these absolute values (i) to the zolpidem reimbursement data and (ii) to the total number (all substances) of annual cases reported to the FAN.

- We described place of zolpidem among all drugs listed on falsified prescriptions during the 3-year period before the measure and the 3-year period after the regulatory change.

### Zolpidem NOTS characteristics

We compared the well-informed NOTS including zolpidem as a suspected drug reported to the FAN during the 3-year period before and the 3-year period after the regulatory change. We used the following criteria for comparisons:

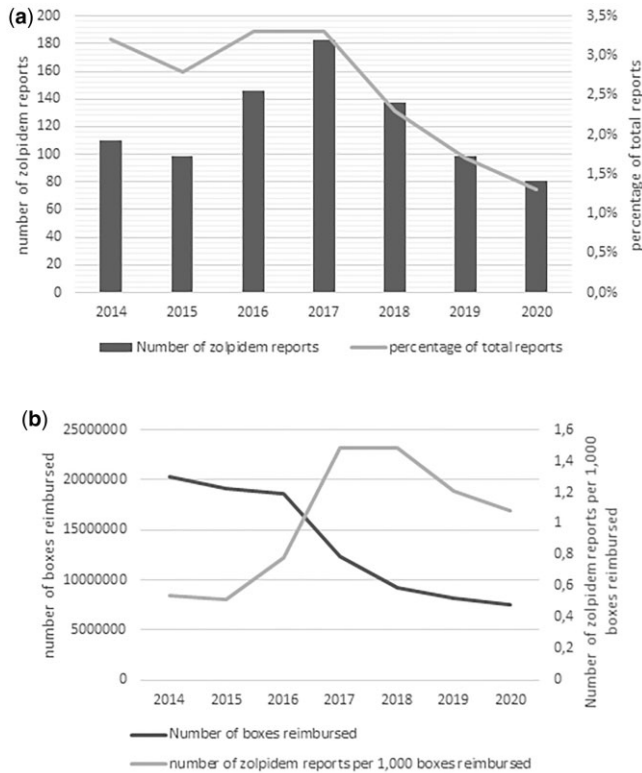
- Patient-related factors:
  - i. Age and gender.
  - ii. Vulnerability factors present in notifications i.e. the presence of at least one risk factor for a substance use disorder and/or a history of a psychiatric disorder and/or the presence of 'related substances' defined as the concomitant use of a substance (medication, illicit substance and alcohol) classified as suspected and/or reported dependence.
  - iii. Unlawful method of obtention: nomadism (medical or pharmaceutical) and/or prescription falsification and/or any other method of illicit procurement.
- Items marking use outside the SPC mentions:
  - i. Overuse, whether mentioned as a reason for declaration and/or calculated (maximum daily dose or maximum dose per intake >10 mg per day for subjects under 65 years of age and 5 mg per day for those over 65 years of age; when the daily dose consumed was variable, the dose used for the calculation was the maximum daily dose consumed).
  - ii. Anteriority of consumption, defined as the minimum exposure time to zolpidem known at the time of notification.
  - iii. Misuse, whether mentioned as reason for declaration and/or defined as use by an unapproved route of administration and/or when at least one effect other than a hypnotic effect was sought and/or in the case of daytime use (at least one dose during the day). Non-hypnotic effects were classified into two categories based on the terms used in the notification: 'calming effects' and 'stimulating effects'. Problematic users who met at least one misuse criterion were defined as 'misusers'; other problematic consumers were defined as 'nonmisusers'.

### Statistical analysis

The evolution of zolpidem volume and importance was presented per year from 2014 to 2020. A description of zolpidem NOTS characteristics was performed for the two periods in the total population and, for each period, according to the status of misuse. Quantitative and qualitative analysis of notification characteristics were performed using continuous data expressed as the means and categorical data as numbers and percentages. Comparisons were used to assess evolution over time and were performed using standard tests (chi-squared test for proportions and Student's *t*-test for means). Statistical significance was fixed at  $P < 0.05$ . All analyses were carried out using R software version 4.2.

### Ethical considerations

French health professionals have the legal obligation, mentioned in the Public Health Code, to report to the FAN cases of abuse or dependence involving a psychoactive substance. These data are recorded anonymously in a national database. FAN pharmacologists are commissioned by the health authorities to analyze these cases of abuse and dependence.



**Figure 1** (a) Absolute number of zolpidem notifications per year and number of zolpidem notifications related to the total number of notifications reported to the FAN. (b) Number of zolpidem notifications relative to the number of boxes reimbursed per year.

## Results

### Zolpidem NOTS volume and importance

Figure 1 shows the number of notifications that included zolpidem received by the FAN per year.

Figure 1a shows that the absolute number of notifications that included zolpidem increased between 2015 (99 notifications) and 2017 (183) before gradually decreasing to 81 notifications in 2020. The proportion of these notifications in the total number of reports to the FAN remained relatively stable from 2014 (3.2%) to 2017 (3.3%) before significantly decreasing until 2020, when it reached its lowest level (1.3%) ( $P < 0.01$ ).

Figure 1b shows the number of notifications in relation to the number of zolpidem boxes reimbursed according to the year. The reimbursement of zolpidem in community pharmacies remained relatively stable in 2014 and 2015 and then began to decline. The most substantial decrease in reimbursement occurred between 2016 and 2018, from 18 626 504 boxes to 9 209 357 boxes (down 52%). Over the 3-year period before the measure was implemented, 58 054 168 boxes of zolpidem were reimbursed vs. 24 896 772 boxes over the 3-year period after the measure was implemented (decrease of ~57%). The proportion of reports that included zolpidem gradually increased between 2014 and 2017 and then decreased between 2018 and 2020 (respectively 1.488 and 1.079 per 1000 reimbursed boxes).

Figure 2 shows the most cited drugs in the OSIAP tool by year from 2014 to 2020: before (figure 2a) and after (figure 2b) the measure.<sup>14</sup>

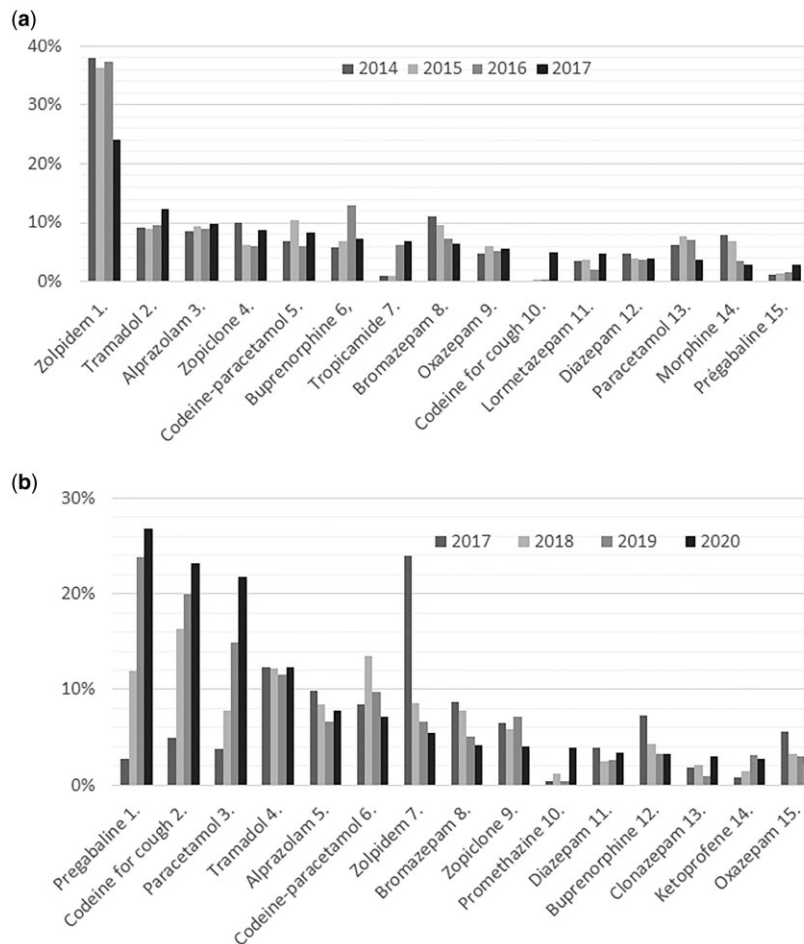
Appearing on more than one-third of falsified prescriptions in the period before the measure was implemented, zolpidem was still the first drug cited in 2017. Zolpidem moved to seventh place after the regulatory measure was implemented and was cited in only 5.4% of falsified prescriptions in 2020 vs. more than 35% in 2016.

### Zolpidem NOTS characteristics

Table 1 presents all the items evaluated according to the period and, in each period, according to the status of misusers or non-misusers.

- i. Overall analysis of NOTS reported to the FAN before and after the measure. The number of NOTS reported over the two periods of equivalent duration was comparable (245 vs. 214). Concerning the patient-related factors reported, comparing the 3-year period after the measure vs. the 3-year period before the measure, the mean age of consumers was slightly higher (43.3 vs. 42.6), as was the proportion of women (53.5% vs. 49.4%), and patients tended to have more vulnerability factors (76.6%,  $n = 164$  vs. 69.0%,  $n = 169$ ,  $P = 0.07$ ), particularly regarding the consumption of related substances (66.8%,  $n = 143$  vs. 57.9%,  $n = 142$ ,  $P = 0.05$ ): users mentioned in the NOTS in the period after the measure consumed significantly more frequently controlled substances ( $P < 0.01$ ) and alcohol ( $P < 0.01$ ) and had significantly more reported diagnoses of dependence ( $P = 0.04$ ) than those mentioned before the measure. The unlawful method of obtention increased between the two study periods ( $n = 78$ , 31.8% vs.  $n = 87$ , 40.6%) ( $P = 0.05$ ). In more than two-thirds of cases, it involved nomadism, mostly medical in both periods. Falsified prescriptions (28.9% before the measure vs. 10.3% after) and street shopping and obtention on the internet seemed relatively stable. The other unlawful methods of obtention mentioned in our NOTS seemed to be on the rise and represented in the period after the measure nearly a third of cases of illicit procurement (illicit procurement by health care facility staff as self-prescription or workplace theft, giving or stealing from a third party, requesting a prescription for a friend or family member or a prescription of convenience, assault or lying to obtain a prescription, overlap of prescriptions and prescription theft). Regarding the items marking the use outside the SPC mentions, comparing the period before the measure vs. the period after the measure, (i) overuse tended to decrease; it was mentioned in 79.2% ( $n = 194$ ) vs. 73.4% ( $n = 157$ ) of the total notifications analyzed, the dose consumed was significantly lower ( $P = 0.02$ ) and the median dose was divided by two in the cases reported (80 mg vs. 40 mg per day); (ii) users subject to notification had a higher median anteriority of use (72 months vs. 84 months); and (iii) the proportion of misusers increased significantly: 43.6% ( $n = 107$ ) vs. 59.3% ( $n = 127$ ) ( $P < 0.01$ ).
- ii. Focus on the NOTS reported to the FAN that mentioned misuse. Comparing misusers vs. non-misusers in both periods, misusers were mostly men, significantly younger ( $P < 0.01$ ) and appeared to have more risk factors for substance use disorder than non-misusers. About three-quarters of them presented at least one risk factor for substance use disorder, mainly the consumption of related substances. Over the two periods, the median dose consumed by misusers was three times higher than the median dose consumed by non-misusers. The median anteriority remained more than 30 months lower than the values reported among non-misusers over the two periods. Regarding misuse for unapproved indication, in a third of cases regardless of the period, at least one effect other than hypnotic was sought. Non-hypnotic effects were classified into two categories based on the terms used in the notification: ‘calming effects’ (anxiolytic, amnesia, antidepressant, analgesic, self-treatment, descent or replacement, potentiating association with buprenorphine, alcohol, benzodiazepines and zopiclone) and ‘stimulating effects’ (stimulant and recreational). When an effect other than hypnotic was sought, it was calming effects in nearly three-fourth of cases (69.3%,  $n = 61$  in the period after the measure and 73.1%,  $n = 57$  in the period before). In both periods, the most sought-after non-hypnotic effect remained the anxiolytic effect. Comparing the period after the measure vs. the period before the measure among misusers, there was a significant decrease in the dose consumed ( $P < 0.01$ ) in the NOTS reported to the FAN; the median dose was divided by more





**Figure 2** (a) The most cited drugs in the OSIAP tool before the implementation of the measure. (b) The most cited drugs in the OSIAP tool after the implementation of the measure.

than two (60 mg vs. 140 mg per day), 75% of misusers consumed at most 140 mg per day after the measure vs. 270 mg per day before the measure and the median anteriority increased (72 months vs. 48 months). Misuse for both an unapproved route of administration (13.1% vs. 9.4%) and an unapproved indication (41.1% vs. 31.8%) tended to increase. There was a more marked use of the IV route than the nasal route (78.6% and 14.3% vs. 60.9% and 30.4%, respectively). When an effect other than hypnotic was sought, the use as a descent or replacement substance increased (5.1% vs. 13.6%,  $P=0.03$ ); stimulating effects were sought in 30.1% ( $n=27$ ) and 26.9% ( $n=21$ ) of cases, respectively. The proportion of daytime intake decreased (39.7% vs. 23.9%,  $P=0.03$ ) but remained at a high level. Among problematic zolpidem users mentioned in our NOTS, there was an increase after the measure in the use of benzodiazepines and zopiclone ( $P=0.02$ ), controlled substances ( $P<0.01$ ) and alcohol ( $P<0.01$ ), and misusers appeared to have more diagnoses of dependence ( $P=0.05$ ) than before the measure was implemented.

## Discussion

### *A necessary measure that had an immediate impact*

The regulatory change had two immediate consequences in quantitative terms: a sharp decline in falsified prescription and a decrease in French reimbursement data for zolpidem. Thus, falsified prescriptions have decreased in a large proportion and in first place in OSIAP since 2011, zolpidem moved to seventh place in the period after the measure. An unlawful method of obtention was still reported in approximately one-third of the cases, which may be

related to the difficulty of falsifying secure prescriptions. Regarding the decrease in the exposure of the population to zolpidem, our results show a decline of ~57% in the number of boxes reimbursed in community pharmacies between the period before the measure and the period after; this may come from a decrease in the number of consumers, which was also found in other studies,<sup>15-17</sup> but also from the decrease in the quantity consumed shown by our results. The number of reports of addictovigilance that included zolpidem relative to reimbursed data increased until 2018, before starting a slow decline. Nevertheless, these data should be compared with the total number of notifications of the network (all substances) in constant increases. Furthermore, the peak of notifications in 2017 might be linked to an announcement effect after a period of underreporting, all the more marked as the profile of abuse and misuse of zolpidem was known. In addition, the reimbursement data give the number of boxes and not the number of consumers, unlike notifications; the ZORRO historical cohort study, whose objective was to evaluate the impact of the change in the regulatory framework for zolpidem on the prescription of zolpidem and other sedative medications, considered the number of consumers by using data from the Generalist Sample of Beneficiaries (6). Thus, the proportion of notifications that included zolpidem in the total number of reports to the FAN reached its lowest level in 2020 (1.3%).

The change in regulation has therefore had an overall impact on all users, problematic consumers or not, misusers or not; otherwise, the number of notifications that included zolpidem would not have decreased as much. The overall decrease in the exposure of the population to zolpidem has implied less initiation of treatment<sup>17,18</sup> and therefore a decrease in the number of users who initiate problematic use. The dose consumed after the regulatory change is also a marker

**Table 1** Evolution of the criteria studied in the NOTS reported to the FAN between the 3-year period before the measure (2014–16) and the 3-year period after the measure (2018–20)

			Total		Misusers		Non-misusers	
			Period before the measure	Period after the measure	Period before the measure	Period after the measure	Period before the measure	Period after the measure
Patient-related factors	Age and gender	Number of reports	245	214	43.6% (107)	59.3% (127)	56.4% (138)	40.7% (87)
		Mean age, years ( <i>n</i> )	42.6 (239)	43.3 (209)	37.9 (106)	40.2 (125)	46.2 (133)	47.8 (85)
	Vulnerability factors	Female, % ( <i>n</i> )	49.4% (120)	53.5% (114)	48.6% (52)	48.0% (61)	49.3% (68)	60.9% (53)
		Presence of at least one risk factor for substance use disorder, % ( <i>n</i> )	69.0% (169)	76.6% (164)	74.8% (80)	81.1% (103)	64.5% (89)	70.1% (61)
		Medical history of psychiatric disorders, % ( <i>n</i> )	36.7% (90)	41.6% (89)	40.2% (43)	44.9% (57)	34.1% (47)	36.8% (32)
		Related substances, % ( <i>n</i> )	57.9% (142)	66.8% (143)	64.5% (69)	70.1% (89)	52.9% (73)	62.1% (54)
		BZD or zopiclone, % ( <i>n</i> )	35.9% (88)	44.4% (95)	36.4% (39)	41.7% (53)*	35.5% (49)	48.3% (42)
		Opioids (analgesics and/or maintenance treatment), % ( <i>n</i> )	20.8% (51)	28.5% (61)	20.6% (22)	26.8% (34)	21.0% (29)	31.0% (27)
		Controlled substances, % ( <i>n</i> )	13.1% (32)	27.1% (58)*	14.9% (16)	35.4% (45)*	11.6% (16)	14.9% (13)
		Alcohol, % ( <i>n</i> )	7.7% (19)	19.6% (42)*	10.3% (11)	25.2% (32)*	5.8% (8)	11.5% (10)
Items marking use outside the scope of the SPC	Dependence, % ( <i>n</i> )	Dependence, % ( <i>n</i> )	39.6% (97)	49.1% (105)*	31.8% (34)	44.1% (56)	45.6% (63)	56.3% (49)
		Unlawful way of obtention, % ( <i>n</i> )	31.8% (78)	40.6% (87)*	44.9% (48)	38.6% (49)	35.5% (49)	43.7% (38)
	Dose	Number of available data	182	148	74	84	108	64
		Med [IQR], mg/day	80 [20–200]	40 [20–140]**	140 [50–270]	60 [23.75–140]	40 [20–140]	20 [20–77.5]
	Anteriority of consumption	Min. to max., mg/day	2.5–4200	5–5600	5–2000	5–1220	2.5–4200	5–5600
		Number of available data	112	95	51	51	61	44
	Misuse	Med [IQR], month	72 [36–120]	84 [36–138]	48 [24–96]	72 [27–120]	84 [48–132]	102 [36–159]
		Min. to max., month	0–456	0–528	0.5–408	0–300	0–456	12–528
	Unapproved route of administration, % ( <i>n</i> )	Unapproved route of administration, % ( <i>n</i> )	9.4% (23)	13.1% (28)	21.5% (23)	22.0% (28)	–	–
		Unapproved indication, % ( <i>n</i> )	31.8% (78)	41.1% (88)	72.9% (78)	69.3% (88)	–	–
Misuse without further information ( <i>n</i> )	Misuse without further information ( <i>n</i> )	6.1% (15)	9.3% (20)	14% (15)	15.7% (20)	–	–	

\*:  $P < 0.05$  using Chi-squared test.

\*\* :  $P < 0.05$  using Student's *t*-test.

BZD, benzodiazepines; IQR, interquartile range.

of better use of zolpidem.<sup>18</sup> If overuse was still mentioned in more than 70% of the total notifications that included zolpidem after 2017, the median dose consumed in the period before the regulatory change was divided by two after its implementation.

### *A persistence of the problems*

However, for the 42% of chronic zolpidem users who continued their consumption after the regulatory change (6), the risk of abuse and dependence is still present.

Markers of problematic consumption persisted after the change in regulation in the NOTS, and two distinct populations of consumers were already identified.<sup>6,7,9</sup> The first was ‘misusers’ (59.3% in 2018–20), whose proportion increased substantially in 2018–20 compared to 2014–16, who consumed zolpidem by an unapproved route of administration—mainly IV—and/or in search of at least one effect other than hypnotic or anxiolytic in more than a third. Experimental studies have shown that the sedative effect of zolpidem occurs at lower doses than those necessary to achieve anticonvulsant, muscle relaxant and anxiolytic effects. This could be explained by a dose-dependent loss of selectivity for the  $\alpha 1$  subunit of GABA-A receptors, which are responsible for the sedative effect. Zolpidem could then bind to subunits of lower affinity, including  $\alpha 2$  and  $\alpha 3$ , which are involved in the occurrence of the anxiolytic effect.<sup>5</sup> The second population, ‘nonmisusers’, took zolpidem for hypnotic purposes without deviating from the typical route of administration. These were chronic users (75% of them had been consuming zolpidem for more than 3 years) of high doses (75% of them consumed more than 20 mg per day regardless of the period), and more than half of them had a diagnosis of dependence in 2018–20.

Data from the NOTS over the two periods appeared to show worsening cases after the regulatory change, in particular for people who were genuinely dependent and/or had comorbidities or misusers for whom zolpidem was the substance of interest. Thus, over the period after the measure, there was a significant increase in vulnerability factors and a tendency to have a longer duration of consumption compared to the period before the measure. Similar results are reported in the literature with other tools. For example, Istvan et al.,<sup>18</sup> in a study conducted in the general population, showed that the regulatory change had a predominantly quantitative impact: if the number of potential problematic users decreased in absolute value after the regulatory change, the profile of these users remained similar before and after the measure. Nevertheless, our data seemed to show a worsening of the cases reported in the period after the implementation of the measure, especially in terms of the vulnerability of patients. Finally, it seems that some populations (such as older subjects) had more difficulty stopping their zolpidem consumption.<sup>19</sup>

### *A report of the problem?*

Furthermore, according to Istvan et al., since the regulatory change, 21% of chronic zolpidem users have replaced zolpidem with zopiclone (6). Rousselot et al.<sup>20</sup> also found that the preferential substitution, when there was replacement, was zopiclone. Zopiclone presents an abuse, dependence and misuse profile that seems less problematic than that for zolpidem.<sup>8,9</sup> A more in-depth study of the addictovigilance data of zopiclone therefore seems necessary to evaluate the impact of this substitution and the possible appearance of new problematic uses for zopiclone.

### *Strengths and limitations*

This national study presents an analysis of the cases of problematic consumption of zolpidem on the basis of clinical and consumption data, which provides complementary information to studies based on medico-administrative data.

The main limitation of this methodology is the non-exhaustiveness of the data: although mandatory, reporting by health

professionals is spontaneous, and we have no notion of the total number of zolpidem consumers. Even if reported cases to the FAN might not necessarily represent all zolpidem consumption, the most serious or unexpected are preferably reported over non-serious cases, and this system remains a good whistleblower.

## Conclusions

These results underline the importance of (i) the continuation of further monitoring for zolpidem; (ii) communication to reduce the prescription of zolpidem in particular and hypnotics in general; (iii) prescriptions in accordance with the recommendations; and (iv) encouraging practitioners to investigate the real effect sought by patients when taking zolpidem.

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## Disclaimer

The content of this article is the sole responsibility of its authors and is not validated by ANSM.

## Key points

- As a result of an increase in abuse, misuse and dependence, the prescription rules of zolpidem, one of the most prescribed hypnotic drugs in France, have been changed in 2017.
- All cases of drug dependence or abuse reported by French health professionals over 3 years before and after 2017 have been analyzed to assess the impact of this regulatory change on the patterns of use of zolpidem in this report.
- This work highlights a sharp decline in prescription falsifications, a decrease in the reimbursement data of zolpidem and in the dose consumed, but also persistent markers of problematic consumption, such as misuse.
- These results imply increased vigilance when prescribing zolpidem, but also zopiclone, main molecule of postponement.

*Conflicts of interest:* None declared.

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